(19) Europäisches Patentamt
European Patent Office
Office européen des brevets

(11) Publication number: **0 189 774**
A1

(12) EUROPEAN PATENT APPLICATION

(21) Application number: 86100362.2

(22) Date of filing: 13.01.86

(51) Int. Cl.⁴: C 07 B 43/06
C 07 C 102/00, C 07 D 227/00
C 07 D 247/00, C 07 D 269/00
C 07 D 283/00, C 07 D 325/00
C 07 D 333/00

(30) Priority: 16.01.85 JP 4107/85

(43) Date of publication of application:
06.08.86 Bulletin 86/32

(84) Designated Contracting States:
DE FR GB

(71) Applicant: TOKUYAMA SODA KABUSHIKI KAISHA
1-1 Mikage-cho
Tokuyama-shi Yamaguchi-ken(JP)

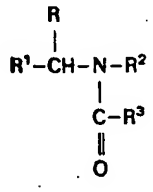
(72) Inventor: Kato, Shozo
1090, Endo Fujisawa-shi
Kanagawa-ken(JP)

(72) Inventor: Okamoto, Hidenori
7-52-1, Shonandai
Fujisawa-shi Kanagawa-ken(JP)

(74) Representative: Kraus, Walter, Dr. et al,
Patentanwälte Kraus, Weisert & Partner
Thomas-Wimmer-Ring 15
D-8000 München 22(DE)

(54) Process for production of N,N-disubstituted carboxylic acid amides.

(57) A novel process for producing N,N-disubstituted carboxylic acid amides represented by the following formula

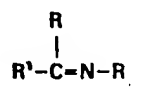


... (1)

wherein

R, R^1, R^2 and R^3 are as defined in claim 1,

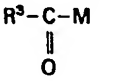
which comprises contacting a Schiff base represented by the following formula (II)



... (II)

wherein

R, R^1 and R^2 are as defined above, with a carboxylic acid derivative represented by the following formula (III)

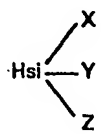


... (III)

wherein

R^3 is as defined above, and M represents a halogen atom or the moiety

in the presence of a silane compound represented by the following formula (IV)



... (IV)

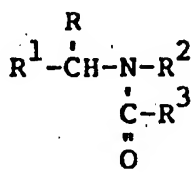
wherein

X, Y and Z, independently from each other, represent a hydrogen atom or a halogen atom,

in the presence or absence of an inert organic solvent.

EP 0 189 774 A1

This invention relates to a novel process for producing N,N-disubstituted carboxylic acid amides of the following formula (I)

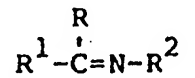


... (I)

wherein R, R^1, R^2 and R^3 are defined below.

Processes for producing N,N-disubstituted carboxylic acid amides of formula (I) which are useful, for example, as medicines, agricultural chemicals, or starting materials or intermediates for producing them are generally known [see, for example, Japanese Laid-Open Patent Publication No. 4181/1985 laid-open on January 10, 1985; U. S. Patents Nos. 2853752, 4372972, 4282028, 4460603, 4521243, 4494978, 4155744, 4456471, 3586496 and 3367847; R. B. Wagner, H. D. Zook, "Synthetic Organic Chemistry", p. 565 (1953), John Wiley & Sons, Inc.; and A. Venkov, M. Nikolova, N. Mollov, Chem. Ind. (London), p. 808 (1982)].

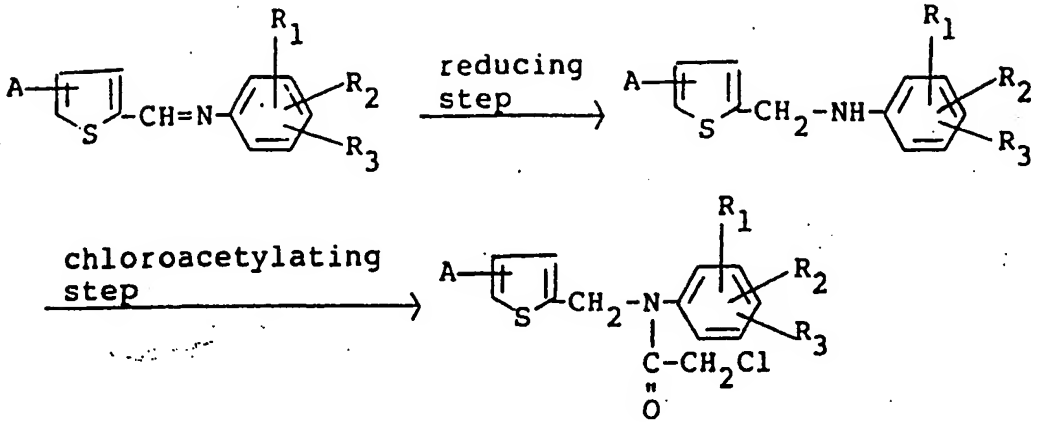
The most general industrial process among them comprises reducing a Schiff base of the following formula (II)



... (II)

wherein R, R^1 and R^2 are as defined below, and acylating or aroylating the resulting reduction product to form a compound of formula (I). For example, the above-cited Japanese Laid-Open Patent Publication No. 4181/1985 discloses a process for producing N,N-disubstituted carboxylic acid amides by a step of reducing the starting Schiff base and a step of chloroacetylating the resulting reduction

product in accordance with the following scheme.

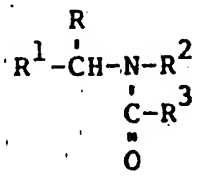


In the above scheme, A represents a hydrogen atom, a halogen atom, an alkyl group, an alkoxy group or an alkylthio group, and R_1, R_2 and R_3, independently from each other, represent a hydrogen atom, a halogen atom, an alkyl group, an alkoxy group or an alkylthio group.

Known processes for producing N,N-disubstituted carboxylic acid amides including the above-exemplified process have one or more defects. For example, they have complex manufacturing steps. The compounds used as starting materials or intermediates are difficult to obtain, or are unstable. Furthermore, the yields of the desired compounds are low. These defects make it difficult for the known processes to give the desired compounds in goods yields at low cost by simple manufacturing steps.

The present inventors have extensively worked on an improvement in conventional industrial processes for producing N,N-disubstituted carboxylic acid amides which essentially comprise the above two steps, and consequently found that by contacting a Schiff base with a carboxylic acid derivative in the presence of a silane compound, the desired N,N-disubstituted carboxylic acid amide can be produced easily in good yields by a one-step process. The investigations of the present inventors have shown that this novel mode of reaction can be applied to the reaction of a wide range of Schiff bases with a wide range of carboxylic acid derivatives.

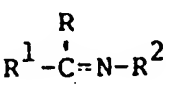
According to this invention, there is provided a novel process for producing N,N-disubstituted carboxylic acid amides represented by the following formula (I)



... (I)

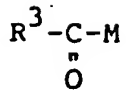
wherein R represents a hydrogen atom, an alkyl group, an alkenyl group, an alkoxy group, an alkenyloxy group, a substituted carbonyl group or a trihalogenomethyl group; R^1, R^2 and R^3, independently from each other, represent a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkenyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group or a substituted or unsubstituted heterocycloalkyl group; R^1 may further represent a hydrogen atom; and R and R^1, taken together, may form a substituted or unsubstituted cyclic group together with the carbon atom to which they are bonded,

which comprises contacting a Schiff base represented by the following formula (II)



... (II)

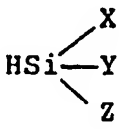
wherein R, R^1 and R^2 are as defined above, with a carboxylic acid derivative represented by the following formula (III)



... (III)

wherein R^3 is as defined above, and M represents a halogen atom or the moiety $-OCR^3$,

in the presence of a silane compound represented by the following formula (IV)

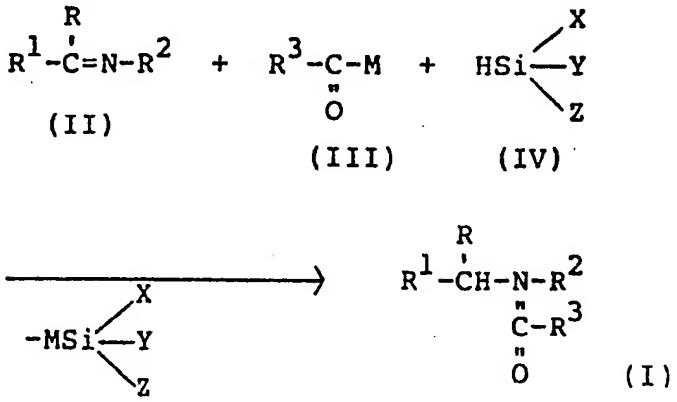


... (IV)

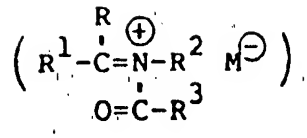
wherein X, Y and Z, independently from each other, represent a hydrogen atom or a halogen atom,

in the presence or absence of an inert organic solvent.

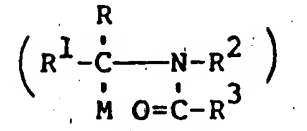
The novel process of this invention can be shown, for example, by the following reaction scheme.



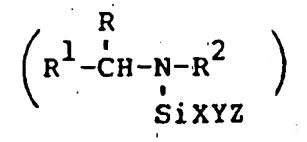
The mechanism of the reaction by which the desired compound of formula (I) is formed in one step by the above novel process is not entirely clear. One possible mechanism presumed by the present inventors is that the Schiff base (II) and the carboxylic acid derivaive (III) react in the presence of the silane compound (IV) to form an immonium salt-type compound



or its M adduct



as an intermediate which further reacts with the silane compound (IV) to form the desired amide compound. Another possible mechanism is that the Schiff base (II) first reacts with the silane compound (IV) to form an N-silyl compound



after which its acylation or arocylation takes place to form the desired amide compound.

It should be understood that the above reaction mechanisms are merely presumed, and do not in any way limit the novel process of this invention, and that the process of this invention includes all embodiments in which the desired compound of formula (I) is formed in one step by "contacting of the compound of formula (II) with the compound of formula (III) in the presence of the compound (IV)" which results in the reaction of these three components.

It has thus been found in accordance with this invention that by the novel mode of reaction, the compound of formula (I) can be produced easily in good yields at low cost with industrial advantage from the compound of formula (II) in one step.

It is an object of this invention to provide a novel process for producing N,N-disubstituted carboxylic acid amides of formula (I).

The above and other objects and advantages of this invention will become apparent from the following description.

According to the process of this invention, the N,N-disubstituted carboxylic acid amides of formula (I) can be produced by contacting the Schiff base of formula (II) with the carboxylic acid derivative of formula (III) in the presence of the silane compound of formula (IV) in the presence or absence of an inert organic solvent.

In formulae (I) and (II), R represents a hydrogen atom, an alkyl group, an alkenyl group, an alkoxy group, an alkenyloxy group, a substituted carbonyl group or a trihalogenomethyl group.

The alkyl group may, for example, be an alkyl group having 1 to 10 carbon atoms, preferably 1 to 6 carbon atoms. Specific examples include methyl, ethyl, propyl, butyl, pentyl, hexyl and octyl groups. The alkenyl group may, for example, be an alkenyl group having 2 to 6 carbon atoms, preferably 2 to 4 carbon atoms. Specific examples of the alkenyl group are vinyl, allyl, propenyl, butenyl, pentenyl and hexenyl groups. The alkoxy group may, for example, be an alkoxy group having 1 to 6 carbon atoms, preferably 1 to 4 carbon atoms. Specific examples of the alkoxy group are methoxy, ethoxy, propoxy, butoxy, pentoxy, hexoxy and octoxy groups. The alkenyloxy group may, for example, be an alkenyloxy group having 2 to 6 carbon atoms, preferably 2 to 4 carbon atoms. Specific examples of the alkenyloxy group are vinyloxy, allyloxy, propenyloxy, butenyloxy, pentenyloxy and hexenyloxy groups. Examples of the substituted carbonyl group are alkylcarbonyl groups having alkyl with 1 to 8 carbon atoms, preferably 1 to 4 carbon atoms, alkoxycarbonyl groups having alkoxy with 1 to 8, preferably 1 to 4 carbon atoms, and arylcarbonyl groups having substituted or unsubstituted aryl having 6 to 10 carbon atoms. In the above aryl carbonyl groups, examples of the substituent for the substituted aryl include alkyl

groups having 1 to 6 carbon atoms, alkenyl groups having 2 to 6 carbon atoms, alkynyl groups having 2 to 6 carbon atoms, alkoxy groups having 1 to 6 carbon atoms, alkylthio groups having 1 to 6 carbon atoms, alkoxycarbonyl groups having 1 to 4 carbon atoms in the alkoxy moiety, alkylcarbonyl groups having 1 to 4 carbon atoms in the alkyl moiety, halogen atoms, a cyano group, a nitro group, dialkylamino groups having 1 to 4 carbon atoms in each alkyl group, trihalogenomethyl groups and alkylcarbonyloxy groups having 1 to 4 carbon atoms in the alkyl moiety. Examples of the aryl group having 6 to 10 carbon atoms are phenyl, naphthyl, tetrahydronaphthyl and indanyl groups.

Thus, specific examples of such substituted carbonyl groups include methylcarbonyl, ethylcarbonyl, propylcarbonyl, butylcarbonyl, methoxycarbonyl, ethoxycarbonyl, propoxycarbonyl, butoxycarbonyl, phenylcarbonyl, naphthylcarbonyl, chlorophenylcarbonyl, bromophenylcarbonyl, fluorophenylcarbonyl, dichlorophenylcarbonyl, chlorofluorophenylcarbonyl, methoxyphenylcarbonyl, ethoxyphenylcarbonyl, methylthiophenylcarbonyl, cyanophenylcarbonyl, nitrophenylcarbonyl, (methylcarbonyloxy)phenylcarbonyl, (trifluoromethyl)phenylcarbonyl, (diethylamino)phenylcarbonyl, (ethoxycarbonyl)phenylcarbonyl, chloronaphthylcarbonyl, and ethoxynaphthylcarbonyl groups. Examples of the trihalogenomethyl group for R are trihalogenomethyl groups in which the halogen is selected from Cl, Br, I and F. Specific examples of such trihalogenomethyl groups are trichloromethyl, tribromomethyl and trifluoromethyl groups.

In formulae (I), (II) and (III), R^1, R^2 and R^3, independently from each other, represent a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkenyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group or a substituted or

unsubstituted heterocycloalkyl group; R^1 may further represent a hydrogen atom; and R and R^1, taken together, may form a substituted or unsubstituted cyclic group together with the carbon atom to which they are bonded.

Preferred examples of R^1, R^2 and R^3 include substituted or unsubstituted alkyl groups having 1 to 15 carbon atoms, preferably 1 to 10 carbon atoms, substituted or unsubstituted alkenyl groups having 2 to 15 carbon atoms, preferably 2 to 10 carbon atoms, substituted or unsubstituted alkynyl groups having 2 to 15 carbon atoms, preferably 2 to 10 carbon atoms, substituted or unsubstituted aryl groups having 6 to 20 carbon atoms, preferably 6 to 15 carbon atoms, substituted or unsubstituted heteroaryl groups having 2 to 20 carbon atoms, preferably 2 to 14 carbon atoms, and containing 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur atoms, substituted or unsubstituted cycloalkyl groups having 3 to 20, preferably 3 to 15 carbon atoms, substituted or unsubstituted cycloalkenyl groups having 3 to 20 carbon atoms, preferably 3 to 15 carbon atoms, and substituted or unsubstituted heterocycloalkyl groups having 2 to 20 carbon atoms, preferably 2 to 15 carbon atoms, and containing 1 to 4 hetero atoms selected from nitrogen, oxygen and sulfur atoms.

Examples of the substituted or unsubstituted cyclic group formed by R and R^1 together with the carbon atom to which they are bonded include cycloalkyl groups having 4 to 15 carbon atoms, preferably 5 to 10 carbon atoms, and heterocycloalkyl groups having 4 to 15 carbon atoms, preferably 5 to 10 carbon atoms, and containing 1 to 4 nitrogen, oxygen or sulfur atoms. Specific examples of such cyclic groups are cyclopentyl, cyclohexyl, cycloheptyl, pyrrolidyl, piperidyl, tetrahydrofuryl and tetrahydropyryl groups.

In the illustrated groups for R^1, R^2, and R^3, examples of substituents which they may have include alkyl groups having 1 to 6 carbon atoms, alkenyl groups having 2

to 6 carbon atoms, alkynyl groups having 2 to 6 carbon atoms, alkoxy groups having 1 to 6 carbon atoms, alkylthio groups having 1 to 6 carbon atoms, alkoxycarbonyl groups having 1 to 4 carbon atoms, alkylcarbonyl groups having 1 to 4 carbon atoms, halogen atoms, a cyano group, a nitro group, dialkylamino groups having 1 to 4 carbon atoms in each alkyl moiety, trihalogenomethyl groups and alkylcarbonyloxy groups having 1 to 4 carbon atoms in the alkyl moiety.

More specific examples of the organic groups R^1, R^2 and R^3 which are widely used industrially are given below.

The unsubstituted alkyl groups include linear or branched alkyl groups, such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl and dodecyl.

The substituted alkyl groups include linear or branched haloalkyl groups such as fluoromethyl, trifluoromethyl, chloromethyl, trichloromethyl, chloroethyl, bromoethyl, fluoropropyl, chloropropyl, chlorobutyl, bromopentyl, chlorohexyl, fluorooctyl, trifluoroethyl and heptafluorobutyl; linear or branched alkoxyalkyl groups such as methoxymethyl, methoxyethyl, methoxypropyl, methoxybutyl, methoxypentyl, methoxyhexyl, ethoxymethyl, ethoxyethyl, ethoxypropyl, ethoxybutyl, propoxymethyl, propoxyethyl, propoxypropyl, propoxybutyl, butoxymethyl, butoxyethyl, butoxypropyl, butoxybutyl and pentoxyethyl; phenoxyalkyl groups such as phenoxymethyl, phenoxyethyl, chlorophenoxypropyl and trichlorophenoxypropyl; cyanoalkyl groups such as cyanoethyl, cyanopropyl and cyanobutyl; nitroalkyl groups such as nitroethyl, nitropropyl, nitrohexyl and nitrodecyl; alkylthioalkyl groups such as methylthiomethyl, methylthioethyl, methylthiopropyl, ethylthiomethyl, ethylthioethyl, ethylthiobutyl and propylthioethyl; arylalkyl groups such as phenylmethyl, phenylethyl, phenylpropyl, methylphenylmethyl and chlorophenylmethyl; heteroarylalkyl

groups such as thienylmethyl, thienylethyl, methoxythienylmethyl, furylmethyl, furylethyl, chlorofurylmethyl, pyrrolylmethyl pyrazolylmethyl and pyrazolylethyl; cycloalkylalkyl groups such as cyclopropylmethyl and cyclohexylethyl; and alkoxycarbonylalkyl groups such as methoxycarbonylmethyl, methoxycarbonylethyl, ethoxycarbonylmethyl, ethoxycarbonylethyl and ethoxycarbonylpropyl.

The unsubstituted alkenyl groups include various position isomers of ethenyl, propenyl, butenyl, pentenyl, hexenyl and octenyl.

The substituted alkenyl groups include haloalkenyl groups such as chloroethenyl, fluoroethenyl, bromoporopenyl, chlorobutenyl, chloropentenyl and fluorohexenyl; alkoxyalkenyl groups such as methoxyethenyl, methoxypropenyl, ethoxybutenyl, ethoxyhexenyl and propoxybutenyl; and other substituted alkenyl groups including cyanoethenyl, cyanopropenyl, nitropropenyl, dimethylaminoethenyl, furylethenyl and methylthiopropenyl.

The unsubstituted alkynyl groups include ethynyl, propynyl, butynyl, pentynyl and hexynyl.

The substituted alkynyl groups include chloropropynyl, bromobutynyl, methoxybutynyl, cyanopropynyl and methylthiobutynyl.

The unsubstituted aryl groups include phenyl, naphthyl anthranyl and phenanthrenyl.

The substituted aryl groups include alkylphenyl groups such as methylphenyl, dimethylphenyl, ethylphenyl, diethylphenyl, propylphenyl, dipropylphenyl, butylphenyl, pentylphenyl, hexylphenyl, methylethylphenyl, methylpropylphenyl, ethylpropylphenyl, methylbutylphenyl, di-(bromoethyl)phenyl and (trifluoromethyl)phenyl; halophenyl groups such as fluorophenyl, difluorophenyl, chlorophenyl, dichlorophenyl, bromophenyl, iodophenyl, trichlorophenyl and chlorofluorophenyl; alkoxyphenyl groups such as methoxyphenyl, dimethoxyphenyl, trimethoxyphenyl, ethoxyphenyl, diethoxyphenyl, propoxyphenyl and butoxyphenyl;

substituted phenyl groups such as cyanophenyl, nitrophenyl, chloro(methyl)phenyl, chloro(ethoxy)phenyl, methyl(methoxy)-phenyl, methylthiophenyl, trifluoromethylphenyl, bis(chloro-ethylamino)phenyl, nitro(methyl)phenyl, diphenyl, chloro-(dimethyl)phenyl, (dimethylamino)phenyl, ethynylphenyl, chloro(methoxy)phenyl, methyl(propoxy)phenyl, (chloro-acetyl)phenyl, methyl(butoxy)phenyl, methylcarbonyloxy-phenyl and acetylpenyl; and substituted naphthyl groups such as methylnaphthyl, dimethylnaphthyl, ethylnaphthyl, chloronaphthyl, dichloronaphthyl, methoxynaphthyl, methyl-thionaphthyl, nitronaphthyl and cyanonaphthyl.

The unsubstituted heteroaryl groups include furyl, thienyl, pyrrolyl, pyridyl, pyrimidinyl, benzofuryl, benzothienyl, indolyl, quinolyl, thiazolyl, pyrazolyl, benzothiazolyl, thiadiazolyl and oxazolyl.

The substituted heteroaryl groups include substituted furyl groups such as methylfuryl, dimethylfuryl, ethylfuryl, propylfuryl, chlorofuryl, bromofuryl, methoxy-furyl, ethoxyfuryl, propoxyfuryl, methylthiofuryl, ethyl-thiofuryl and nitrofuryl; substituted thienyl groups such as methylthienyl, ethylthienyl, propylthienyl, butyl-thienyl, fluorothienyl, chlorothienyl, bromothienyl, iodo-thienyl, methoxyethienyl, ethoxythienyl, propoxythienyl, methylthiothienyl, ethylthiothienyl, nitrothienyl, di-chlorothienyl and dimethylthienyl; substituted pyrrolyl groups such as N-methylpyrrolyl, N-ethylpyrrolyl, methyl-N-methylpyrrolyl, chloro-N-ethylpyrrolyl, methoxy-N-methylpyrrolyl, methoxypyrrolyl, ethylpyrrolyl and chloro-pyrrolyl; substituted pyridyl groups methylpyridyl, ethyl-pyridyl, chloropyridyl and methoxypyridyl; substituted benzofuryl groups such as methylbenzofuryl, chlorobenzo-furyl, ethoxybenzofuryl, nitrobenzofuryl, bromo(methoxy)-benzofuryl and chloromethylbenzofuryl; substituted benzo-thienyl groups such as ethylbenzothienyl, fluorobenzo-thienyl, methoxybenzothienyl, nitrobenzothienyl and chlorobenzothienyl; substituted quinolyl groups such

as methylquinolyl, ethylquinolyl, chloroquinolyl and methoxyquinolyl; and other substituted heteroaryl groups including methylthiazolyl, methylindolyl, methylpyrimidyl, methylisothiazolyl, ethylcarbazolyl, dimethylpyrrolyl, methylisoxazolyl, phenylisoxazolyl, methoxydihydropyrimidyl, methylthiazolyl, methyloxadiazolyl, N-methyl-(methylthio)triazolyl, methylthiothiadiazolyl, methylthiazolyl, and methylthiazinyl.

The unsubstituted cycloalkyl groups include cyclopropyl, cyclobutyl, cyclkopentyl and cyclohexyl.

The substituted cyclkoalkyl groups include methylcyclopropyl, ethylcyclopropyl, propylcyclopropyl, chlorocyclopropyl, methoxycyclopropyl, ethoxycyclopropyl, methylcyclobutyl, bromocyclobutyl, methylthiocyclobutyl, chlorocyclopentyl, methylcyclohexyl, ethylcyclohexyl, chlorocyclohexyl, methoxycyclohexyl, propoxycyclohexyl, dimethylcyclohexyl, dichlorocyclopropyl, chlorocyclohexyl, tetrahydronaphthyl and dihydroindanyl.

The unsubstituted cycloalkenyl groups include cyclobutenyl, cyclopentenyl and cyclohexenyl.

The substituted cycloalkenyl groups include methylcyclobutenyl, chlorocyclopentenyl, methoxycyclopentenyl, methylcyclohexenyl, ethylcyclohexenyl, chlorocyclohexenyl, methoxycyclohexenyl, ethoxycyclohexenyl, trimethylcyclohexenyl, dimethylcyclohexenyl, tetramethylcyclohexenyl and propenylcyclohexenyl.

The unsubstituted heterocycloalkyl groups include tetrahydrofuryl, tetrahydrothienyl, pyrrolidyl, tetrahydropyryl, tetrahydrothiopyryl and piperidyl.

The substituted heterocycloalkyl groups include N-methylpyrrolidyl, N-ethylpyrrolidyl, N-methylpiperidyl, dihydropyryl, dimethylpiperidyl, dioxolanyl and N-ethylpiperidyl.

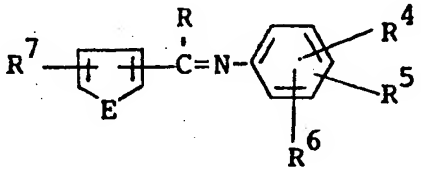
Compounds having the above-listed groups, in many cases, have various position isomers which may equally be used in the practice of the process of this invention without any particular limitation. For example, the

methylphenyl group includes o-methylphenyl, m-methylphenyl and p-methylphenyl groups, and the butyl group includes n-butyl, sec-butyl and tert-butyl groups.

The substituents are not limited to the above specific examples. Any substituents may be used as required so long as they lead to the formation of the carboxylic acid amides of formula (I) contemplated by the process of this invention.

The Schiff bases of formula (II) which are preferred in industrial practice may be grouped into the following compounds.

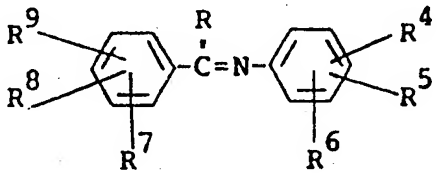
Compounds of the following formula



... (II-1)

wherein E represents O or S, R is as defined above, R^4, R^5, R^6 and R^7, independently from each other, are the same as defined above for R^1, provided that they do not form a cyclic group with R.

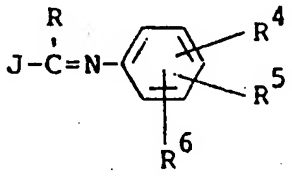
Compounds of the following formula



... (II-2)

wherein R is as defined above, and R^4, R^5, R^6, R^7, R^8 and R^9, independently from each other, are the same as defined above for R^1, provided that they do not form a cyclic group with R.

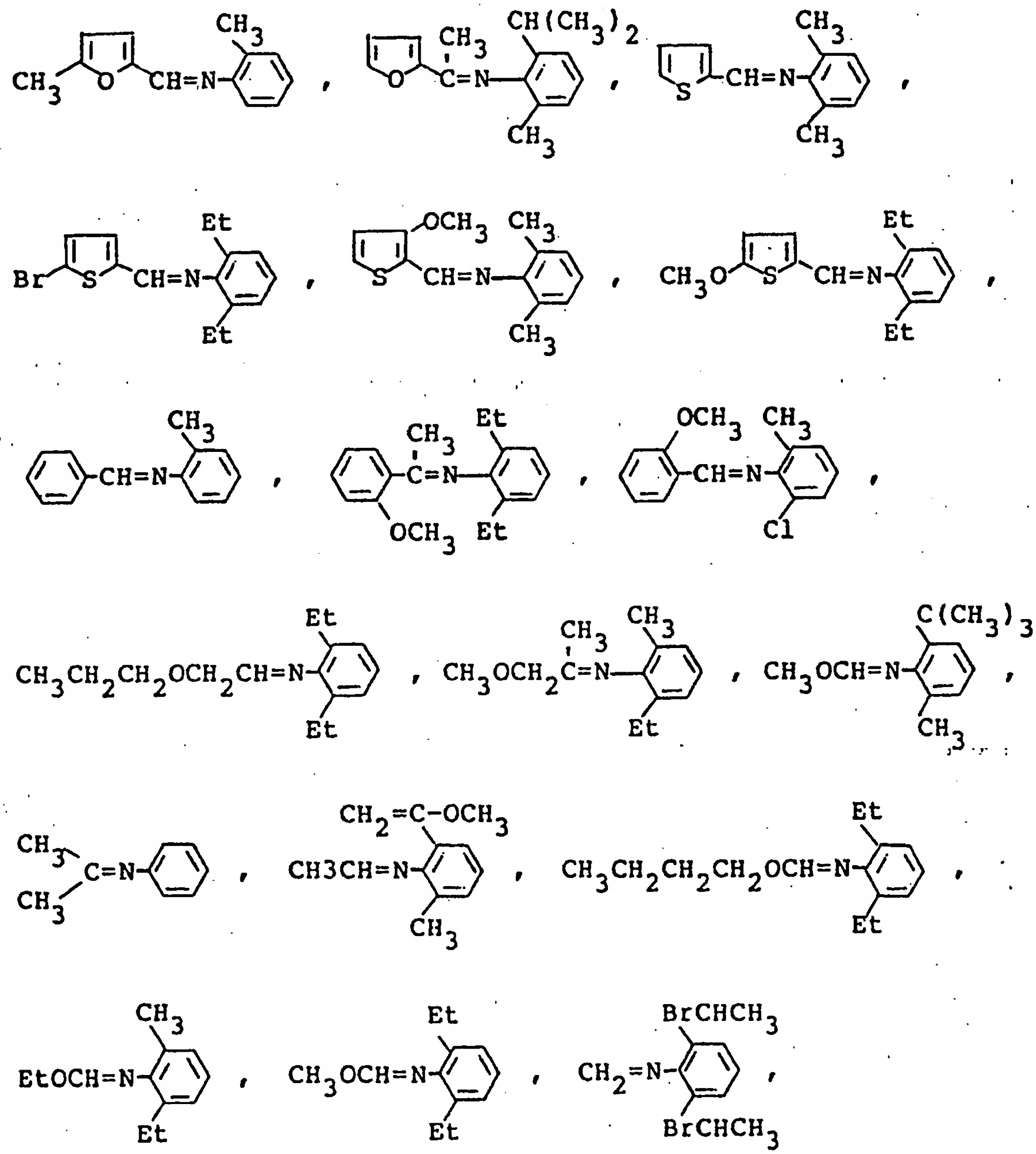
Compounds of the following formula

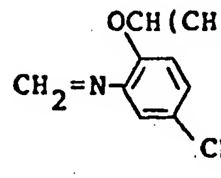
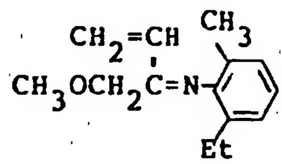
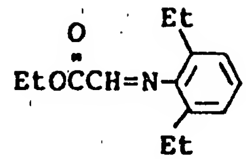


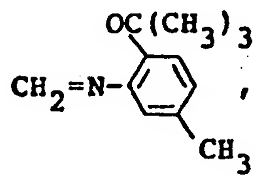
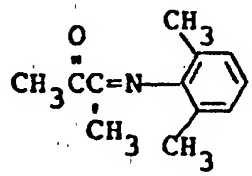
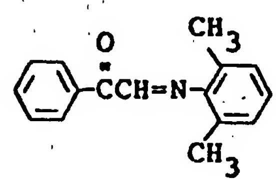
... (II-3)

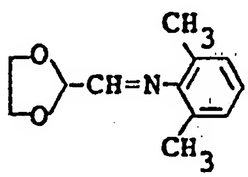
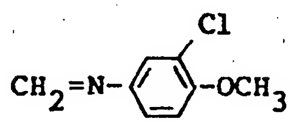
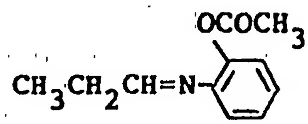
wherein J represents an alkyl, alkoxy, alkoxyalkyl or alkoxycarbonyl group, R is the same as defined above, and R^4, R^5 and R^6, independently from each other, are the same as defined above for R^1.

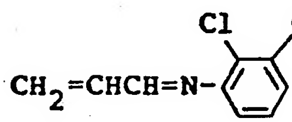
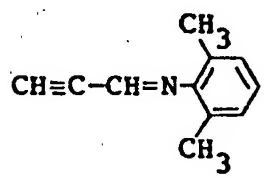
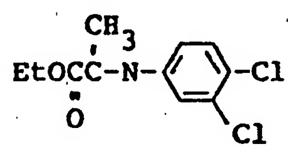
The following compounds may be cited as specific examples of the Schiff base (II) which can be advantageously used in industrial practice. In the following compounds, Et represents an ethyl group.

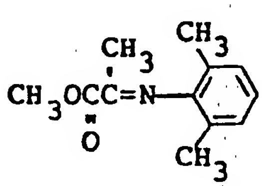
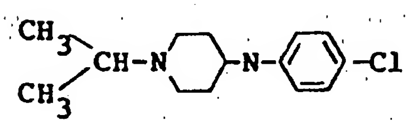
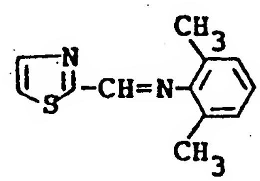


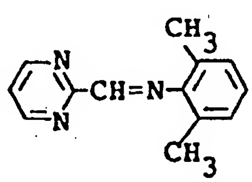
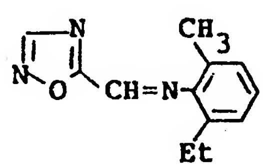
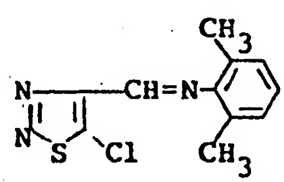
 ,  ,  ,

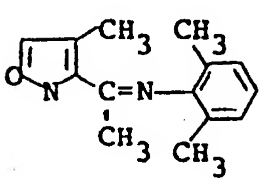
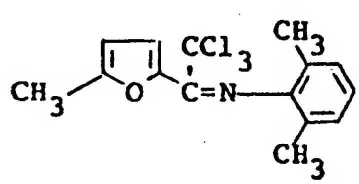
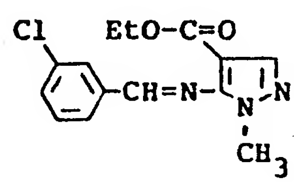
 ,  ,  ,

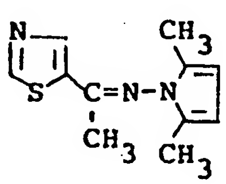
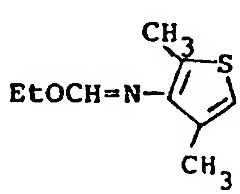
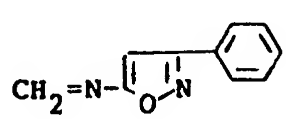
 ,  ,  ,

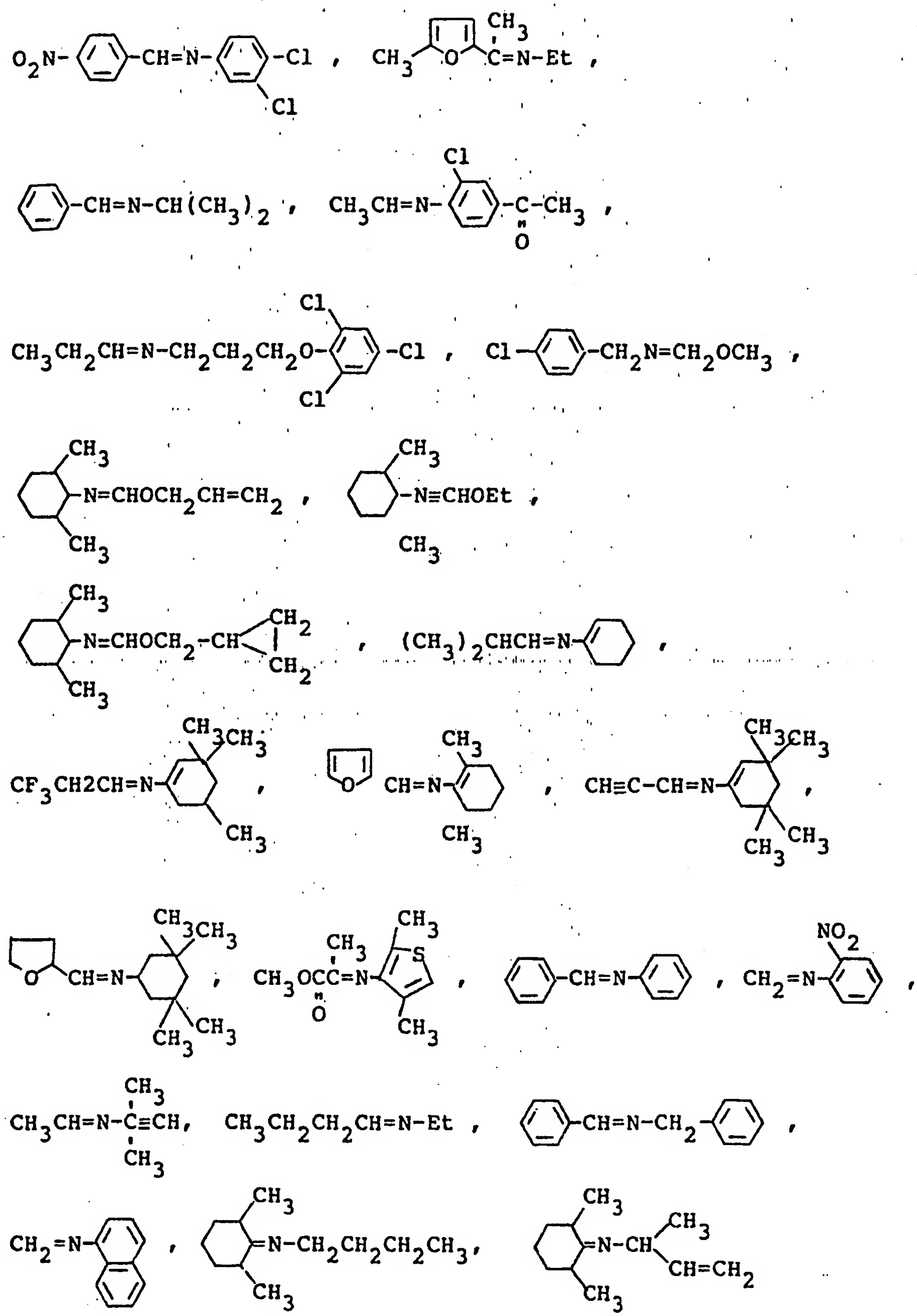
 ,  ,  ,

 ,  ,  ,

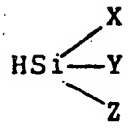
 ,  ,  ,

 ,  ,  ,

 ,  ,  ,



In the silane compound of the following formula (IV)

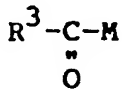


... (IV)

wherein X, Y and Z, independently from each other, represent a hydrogen atom or a halogen atom,

the halogen atom is chlorine, bromine, iodine or fluorine. Chlorine and bromine are preferred. Specific examples of the silane compounds which are preferably used in industrial practice are $HSiCl_3$, $HSiBr_3$, H_2SiCl_2, H_2SiBr_2 and H_3SiBr.

The carboxylic acid derivative of the following formula



... (III)

wherein R^3 is as defined above and M represents a halogen atom or the moiety $-OCR^3$,

is a carboxylic acid halide when M in formula (III) is a halogen atom. Examples of the halogen atom are fluorine, chlorine, bromine and iodine atoms. For industrial practice, carboxylic acid chlorides or bromides of the above formula in which M is a chlorine or bromine atom are especially preferred. When M represents the moiety $-OCR^3$,

the above formula (III) represents a carboxylic acid anhydride $R^3-C(=O)-O-C(=O)-R^3$.

Examples of preferred compounds (III) are compounds of the following formulae (III-1) and (III-2).

Compounds of the formula

$$GCH_2\text{-}\overset{\overset{O}{\|}}{C}\text{-}M \qquad \ldots \text{(III-1)}$$

wherein M is as defined above, and G represents a hydrogen atom, a halogen atom, an alkyl group or an alkoxy group.

Compounds of the formula

$$L\text{-}\overset{\overset{O}{\|}}{C}\text{-}M \qquad \ldots \text{(III-2)}$$

wherein M is as defined above, and L represents a phenyl, pyridyl, furyl or benzyl group.

Examples of the halogen atom for G in formula (III-1) are chlorine, bromine, iodine and fluorine. Examples of the alkyl groups for G are those having 1 to 10 carbon atoms, and examples of the alkoxy group for G are those having 1 to 10 carbon atoms.

Specific examples of the compound of formula (III) include carboxylic acid halides such as acetyl chloride, acetyl bromide, chloroacetyl chloride, dichloroacetyl chloride, bromoacetyl bromide, iodoacetyl chloride, dibromoacetyl chloride, methoxyacetyl chloride, cyanoacetyl chloride, trifluoroacetyl fluoride, propionyl chloride, chloropropionyl chloride, bromopropionyl bromide, butanoyl chloride, chlorobutanoyl chloride, pentanoyl chloride, chloropentanoyl chloride, hexanoyl chloride, acryloyl chloride, butenoyl chloride, chlorobutenoyl chloride, pentenoyl chloride, chloropentenoyl chloride, propyoyl chloride, phenylpropionyl chloride, phenylpropenoyl chloride, furylacryloyl chloride, benzoyl chloride, benzoyl bromide, methylbenzoyl chloride, ethylbenzoyl bromide, chlorobenzoyl chloride, fluorobenzoyl fluoride, methoxybenzoyl chloride, chloro(methyl)benzoyl chloride, cyanobenzoyl chloride, phenylbenzoyl chloride, nitrobenzoyl chloride, furoyl chloride, thiophenecarboxylic acid chloride, indolecarboxylic acid chloride, picolyl chloride,

cyclopropanecarboxylic acid chloride, phenylacetyl chloride, thienylacetyl chloride, dimethylbenzoyl chloride, fluoroacetyl chloride, dibromoacetyl bromide, phenylchloroacetyl chloride, phenyldichloroacetyl chloride, ethoxybutanoyl chloride, cyanopentanoyl chloride, nitropropionyl bromide, methylthiophenecarboxylic acid chloride, pyrazolylacetyl chloride, pyridinecarboxylic acid chloride, methylthiopyridinecarboxylic acid chloride, acetoacetyl bromide, methylthiopropionyl bromide, bromofuranecarboxylic acid bromide, piperidinecarboxylic acid chloride, ethoxycarbonylacetyl chloride, heptafluoropropoxytetrafluoropropionyl fluoride, imidazolecarboxylic acid chloride, and cinnolinecarboxylic acid chloride; and carboxylic acid anhydrides such as acetic anhydride, propionic anhydride, trifluoroacetic anhydride, chloroacetic anhydride and benzoic anhydride.

In the practice of the process of this invention, the reaction may be carried out in the presence or absence of a solvent. Generally, it is preferred to carry it out in an inert organic solvent which does not react with the reactants and the products. Examples of the inert organic solvent include hydrocarbons, halogenated hydrocarbons, and nitriles, such as benzene, toluene, methylene dichloride, chloroform and acetonitrile.

The amounts of the compounds of formulae (II), (III) and (IV) charged in the practice of the process of this invention can be properly selected. For example, the silane compound of formula (IV) is used in an amount of 0.25 to 2.2 moles per mole of the Schiff base of formula (II). This amount may be varied properly depending upon the number of hydrogen atoms which the silane compound of formula (IV) has. For example, when the silane compound of formula (IV) has one hydrogen atom, its amount is 1 to 2.2 moles. Likewise, its amount is 0.5 to 1.7 moles for 2 hydrogen atoms, 0.34 to 1.5 moles for 3 hydrogen atoms, and 0.25 to 0.8 mole for 4 hydrogen atoms. The amount of the

compound of formula (III) is, for example, 1 to 1.2 moles per mole of the Schiff base of formula (II). The amounts of the compounds of formulae (II), (III), and (IV) can be easily set at preferred values by preliminary experiments according to the types of these compounds, the reaction conditions, etc.

If the carboxylic acid derivative of formula (III) is used in too large an amount, side-reactions sometimes tend to occur. Accordingly, it is preferred to determine the mole ratio of the starting materials experimentally before they are actually used in the process.

The Schiff base of formula (II), as one starting material used in the invention, needs not to be a purified one. For example, it is possible to synthesize a Schiff base from an aldehyde and an amine by azeotropic dehydration, etc., and the as-synthesized Schiff base can be reacted directly with the silane compound (IV) and the carboxylic acid derivative (III).

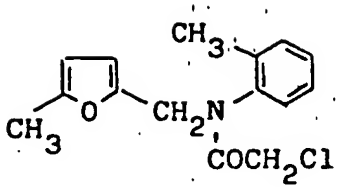
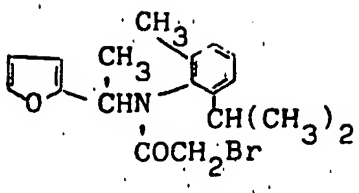
The reaction temperature is not particularly limited, and can be selected from a broad range of temperatures. Preferably, the reaction is carried out at temperatures which are suitable in view of the chemical reactivity of the starting compounds or the stability of the resulting amide compound. Generally, it is selected from a range of $-20^{\circ}C$ to $150^{\circ}C$. The reaction time, which varies depending upon the reaction temperature, may generally be several minutes to several days, for example 5 minutes to 10 days.

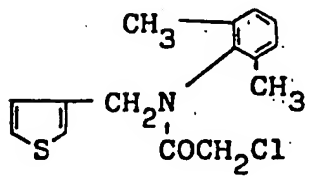
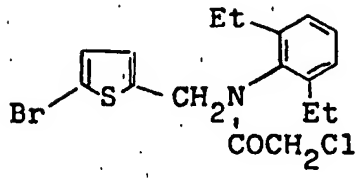
The sequence of addition of the reactants of formulae (II), (III) and (IV) in the process of this invention is not particularly limited. Generally, the silane compound and the carboxylic acid derivative are added to the Schiff base at room temperature or under cooling. It is also possible to add the Schiff base to a solution of the silane compound and the carboxylic acid derivative. In general, a solvent is frequently used in

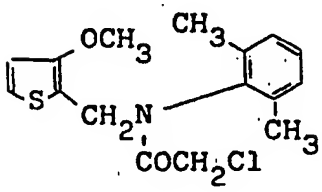
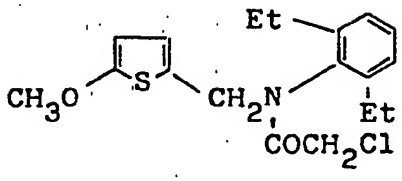
this reaction. For example, it is possible to add the Schiff base, the silane compound and the carboxylic acid derivative to a solvent, and then react the three compounds in it. Alternatively, the three compounds are dissolved in separate solvents and the solutions are mixed for reaction.

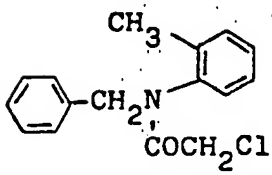
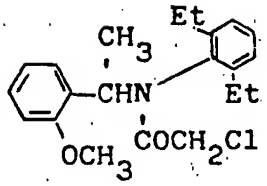
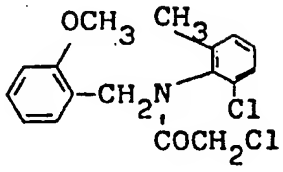
According to this invention, the carboxylic acid amides of formula (I) can be easily obtained by reacting the starting compounds of formulae (II), (III) and (IV). There is no particular limitation on the method of purifying the compound of formula (I) obtained by the above reaction. Generally, after the reaction, the reaction mixture may be distilled under atmospheric or reduced pressure. As required, washing, recrystallization and chromatography may also be used for purification. When the compound (I) obtained has a high boiling point, low-boiling components such as the solvent are removed, and the residue is again dissolved in a solvent. The solution is washed with water and a dilute aqueous alkaline solution, and then the solvent is removed. As a result, the unreacted silane compound and carboxylic acid derivative, a by-product silane compound, etc. can be easily removed, and the desired compound of formula (I) can be obtained in pure form.

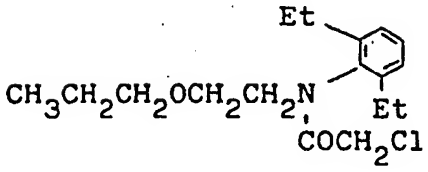
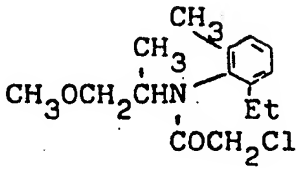
Specific examples of especially useful N,N-disubstituted carboxylic acid amides of formula (I) obtained by the process of this invention are given below. In the following compounds, Et represents an ethyl group.

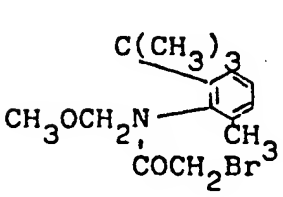
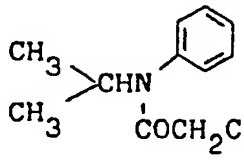
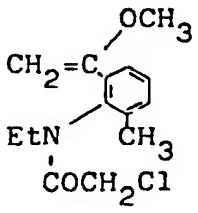

,

,

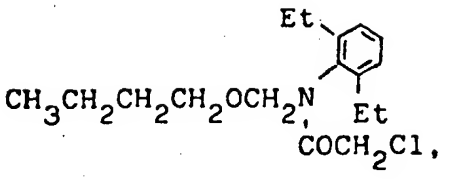

,

,

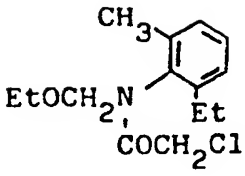

,

,

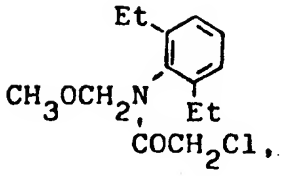

,

,


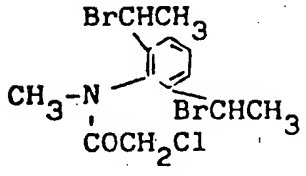

,

,

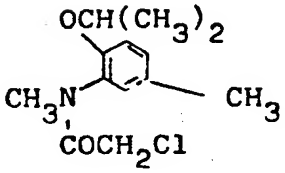

,

,

,

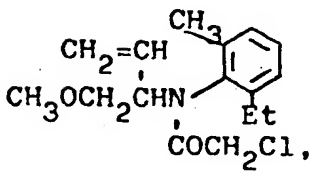


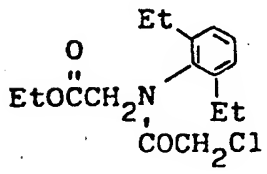


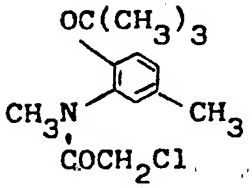


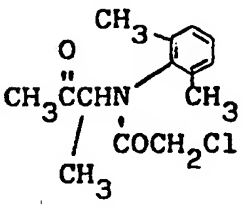


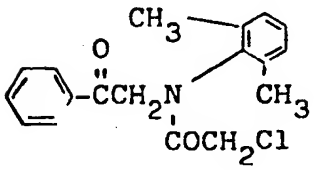


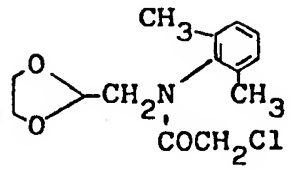


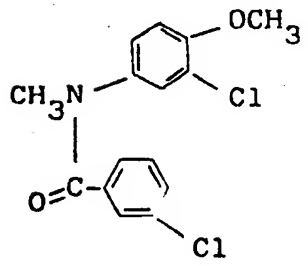


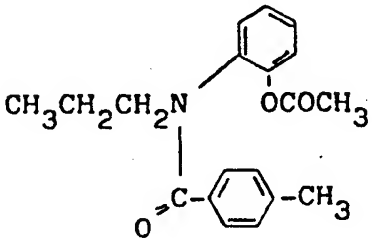


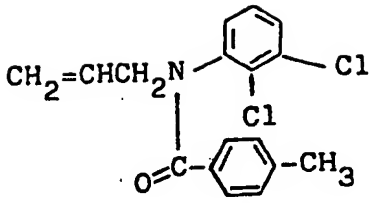




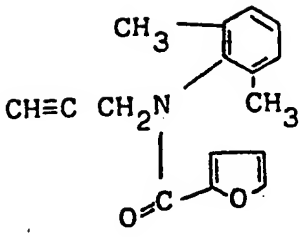




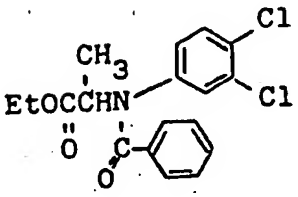




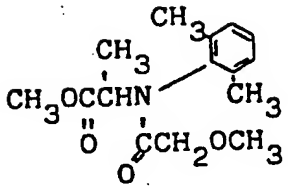
,



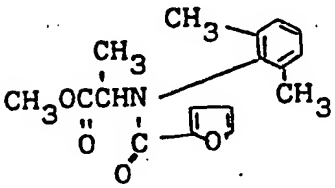
,



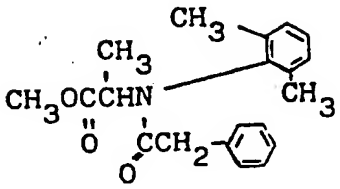
,



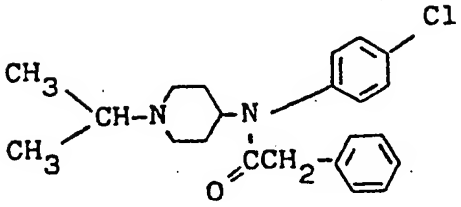
,



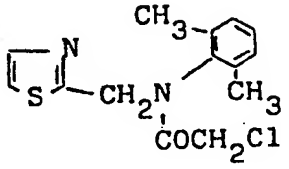
,



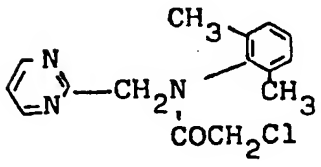
,



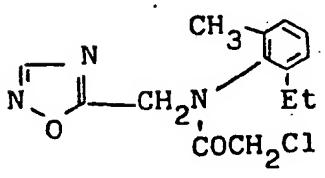
,



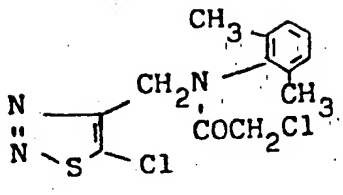
,



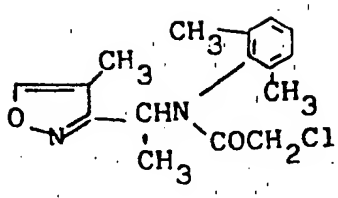
,



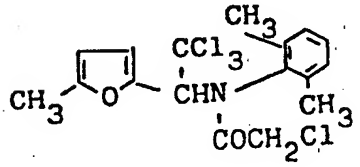
.



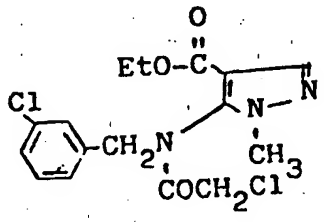
,



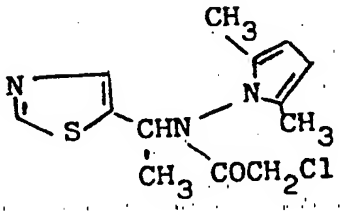
,



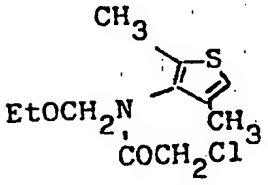
,



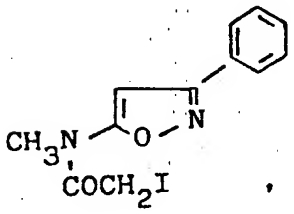
,



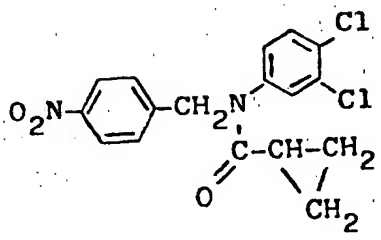
,



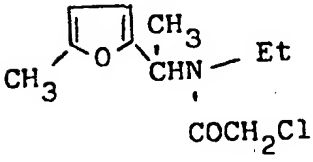
,



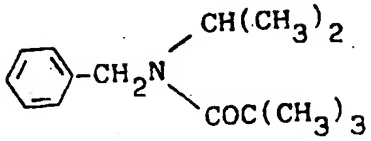
,



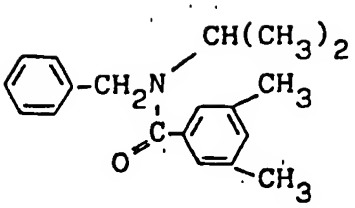
,



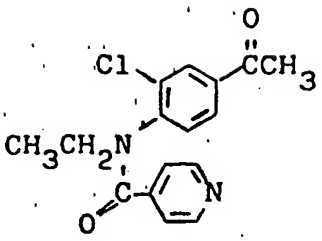
,



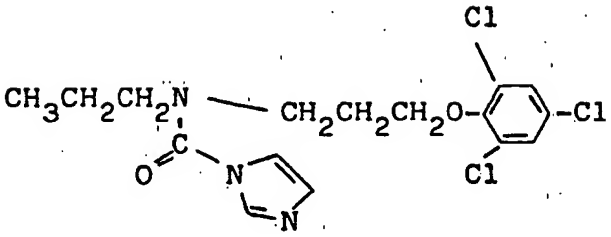
,



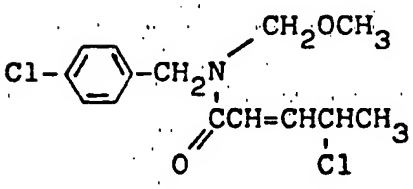
,



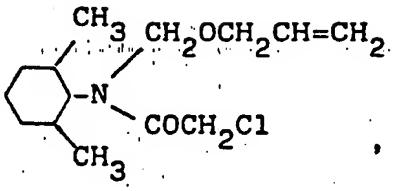
,



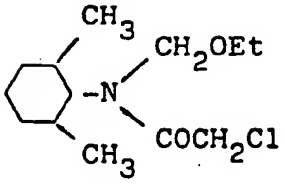
,



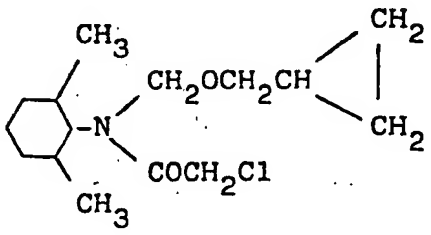
,



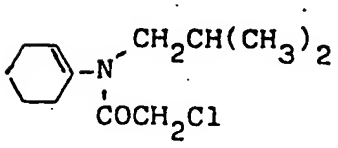
,



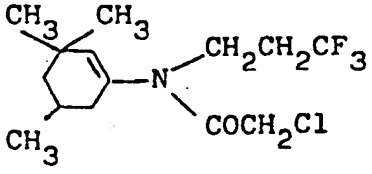
,



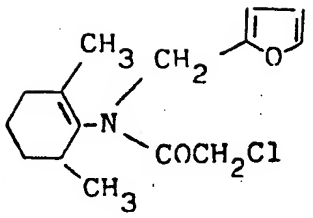
,



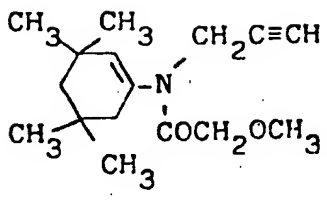
,



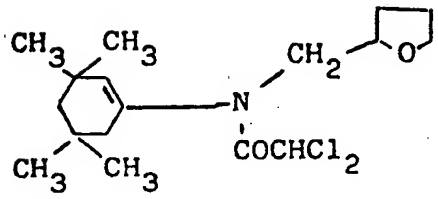
,



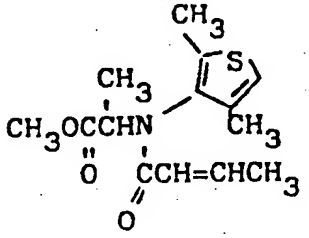
,



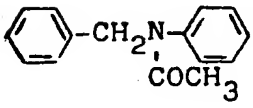
,



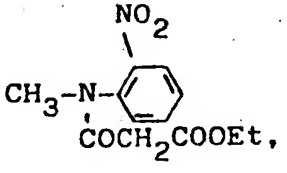
,



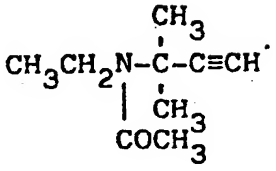
,



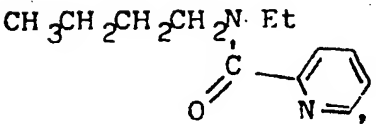
,



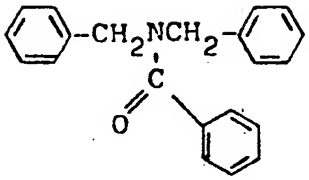
,



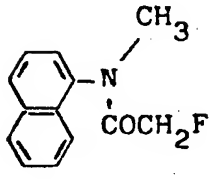
,



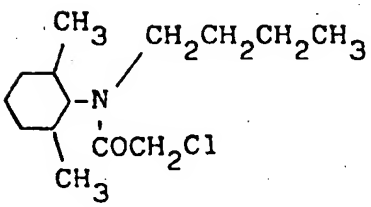
,



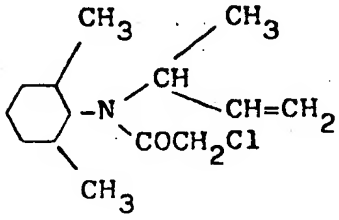
,



,



,



,

The N,N-disubstituted carboxylic acid amides obtained by the process of this invention are known to be useful as medicines and agricultural chemicaas such as herbicides, insecticides or fungicides and intermediates for the production of the medicines and the agricultural chemicals. Accordingly, they can be used in these known applications without any restriction.

The process of this invention is an excellent process for producing N,N-disubstituted carboxylic acid amides useful as medicines and agricultural chemicals in good yields from the corresponding Schiff base compounds in one step under mild reaction conditions. After the reaction, the resulting product can be easily purified. Accordingly, the present invention offers an excellent industrial advantage.

The following Examples illustrate the present invention more specifically. It should be understood that the invention is in no way limited by these examples.

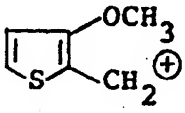
EXAMPLE 1

A three-necked flask was charged with a solution of 2-(3-methoxy)-thienylmethylidene-2',6'-dimethylaniline (2.49 g) in dry benzene (15 ml), and under a nitrogen atmosphere, a solution of trichlorosilane (2.48 g) in dry benzene (5 ml) was gradually added dropwise with stirring at room temperature. Thereafter, a solution of chloroacetyl chloride (1.22 g) in dry benzene (5 ml) was gradually added, and the mixture was stirred at room temperature for 2 hours. Low-boiling components were removed, and the remaining viscous liquid was again dissolved in benzene (50 ml). The benzene solution was washed with water and then with a dilute aqueous alkaline solution, and dried over anhydrous sodium sulfate. Benzene was removed, and the resulting viscous liquid was dried under vacuum to give a pale brown solid (3.30 g). When distilled, this compound had a boiling point of 172°C/0.15 mmHg.

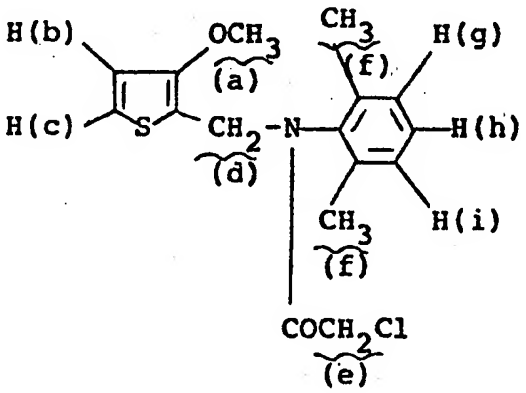
The infrared absorption spectrum of this compound

showed an absorption at 3100 - 2800 cm^{-1} assigned to the C-H bond, and a strong absorption at 1670 cm^{-1} assigned to the carbonyl linkage of the amide group.

Elemental analysis values were C 59.37%, H 5.89%, and N 4.05%, which well agreed with the calculated values for the composition formula $C_{16}H_{18}NSO_2Cl$ (323.84), i.e. C 59.33%, H 5.61% and N 4.33%.

The mass spectrum of the compound showed a molecular ion peak, $M^{\oplus}$, corresponding to the molecular weight at m/e 323, a peak corresponding to M^{+}-Cl at m/e 288, a peak corresponding to $M^{\oplus}-COCH_2Cl$ at m/e 246, and a peak corresponding to  at m/e 127 (100%).

The ^{1}H-NMR spectrum (δ ppm; internal standard tetramethylsilane; deuterochloroform solvent) of the compound was also measured. The results were as follows:-



It shows a singlet at 1.95 ppm for 6 protons corresponding to the methyl protons of (f) substituted at the 2- and 6-positions of the phenyl group; a singlet at 3.50 ppm for 3 protons corresponding to the methyl group of (a); a singlet at 3.72 ppm for 2 protons corresponding to the methylene group of (e); a singlet at 4.75 ppm for 2 protons corresponding to the methylene group of (d); a quadruplet at 6.55 ppm for 2 protons corresponding to the protons of the thiophene ring of (b) and (e); and a multiplet at 7.00-7.45 ppm for 3 group corresponding to the

protons of the benzene ring at (g), (h) and (i).

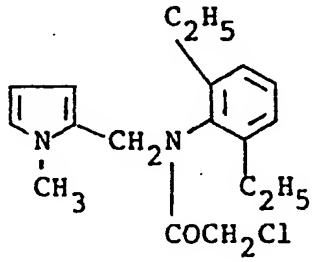
The above results led to the determination that the isolated product was N-[2'-(3'-methoxy)-thienylmethyl]-N-chloroaceto-2,6-dimethylanilide. The yield was 93%.

EXAMPLE 2

The same reaction as in Example 1 was carried out by using acetonitrile as the solvent. After the reaction, low-boiling components were removed, and the resulting viscous liquid was dried in vacuum to form a solid. Recrystallization of the solid from hexane gave N-[2'-(3'-methoxy)-thienylmethyl]-N-chloroaceto-2,6-dimethylanilide as white crystals in a yield of 55%.

EXAMPLE 3

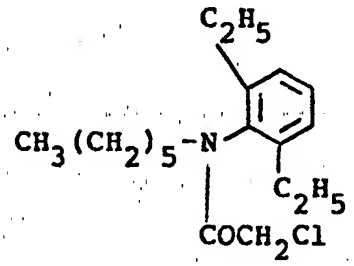
A solution of 2-(N-methylpyrrolyl)-methylidene-2',6'-diethylaniline (2.40 g) in dry benzene (20 ml) was put in a flask. Under a nitrogen atmosphere, a solution of chloroacetyl chloride (1.42 g) in dry benzene (5 ml) was gradually added with stirring at room temperature. Thereafter, a solution of trichlorosilane (2.38 g) in dry benzene (10 ml) was added. After the addition, the mixture was heated with stirring for 1 hour over an oil bath (50°C). Low-boiling components were removed under reduced pressure, and the resulting viscous liquid was purified by column chromatography to give N'-[2-(N-methylpyrrolyl) methyl]-N'-chloroaceto-2',6'-diethylanilide of the following formula as a pale brown solid in a yield of 64%.



EXAMPLE 4

A mixture of n-hexylaldehyde (1.53 g), 2,6-diethylaniline (2.24 g) and benzene (50 ml) was heated under

reflux for 1 hour over an oil bath to perform azeotropic dehydration. To the resulting solution were added a solution of chloroacetyl chloride (1.79 g) in dry benzene (5 ml) and then a solution of trichlorosilane (3.40 g) in dry benzene (5 ml) with stirring at room temperature. After the addition, the mixture was heated with stirring for 2 hours over an oil bath (40°C). Low-boiling components were removed under reduced pressure, and the resulting viscous liquid was dissolved in ether (50 ml). The ether solution was washed with water, and dried over anhydrous sodium sulfate. Ether was removed, and the resulting liquid was distilled to form N-(n-hexyl)-N-chloroaceto-2,6-diethylanilide of the following formula having a boiling point of 152°C/0.2 mmHg in a yield of 55% based on 2,6-diethylaniline.



EXAMPLE 5

In the same way as in Examples 1, 2 and 3, various amide compounds were synthesized using trichlorosilane as the silane compound. The structural formulae, properties and yields of the resulting N,N-disubstituted carboxylic acid amides are summarized in Table 1.

Table 1

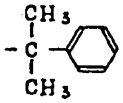
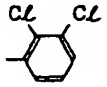
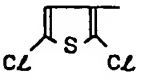
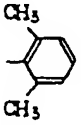
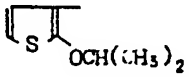
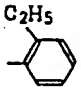
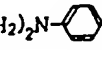
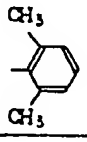
No.	$R^1-CH_2-N(-O-C(=O)-R^3)-R^2$			Property	Yield
	R^1	R^2	R^3		
1	C_5H_7-	$-C_{10}H_{21}$	$-CH_2Cl$	bp. 145℃/0.1mmHg	58
2			$-CF_3$	bp. 115℃/0.4mmHg	50
3				mp. 95~7℃	65
4			$-C_5H_{11}$	bp. 165℃/0.3mmHg	63
5	CH_3O- 	$-CH_2CH_2OCH_3$	$-CH_2Cl$	bp. 160℃/0.15mmHg	48
6			$-CH_2Cl$	bp. 150℃/1.5mmHg	43
7		$-CH_2CH_2OCH_3$	$-CH_2Cl$	bp 116℃/0.25mmHg	51
8			$-CH_2Cl$	bp. 174℃/0.6mmHg	53
9			$-CH_2Cl$	bp. 178℃/0.3mmHg	40
10			$-CH_2Cl$	bp. 169℃/0.2mmHg	38
11	$(Cl-CH_2CH_2)_2N-$ 		$-CH_2Cl$	mp. 83~5℃	45

Table 1 (continued)

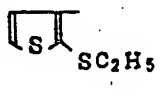
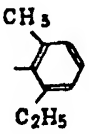
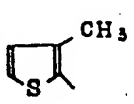
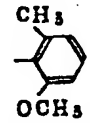
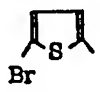
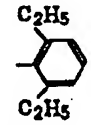
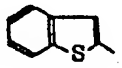
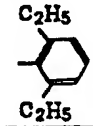
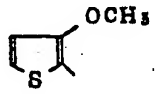
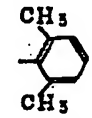
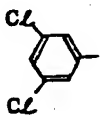
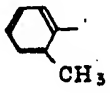
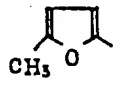
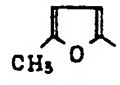
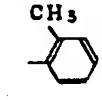
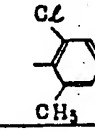
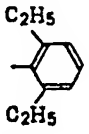
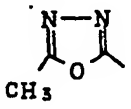
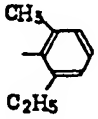
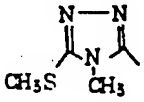
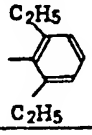
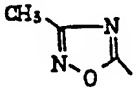
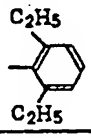
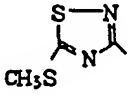
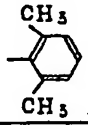
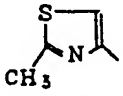
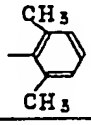
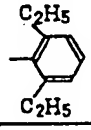
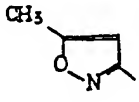
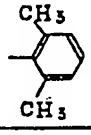
12			$-CH_2C\ell$	bp.188℃/0.4mmHg	60
13			$-CH_2C\ell$	bp.160℃/0.15mmHg	54
14			$-CH_2C\ell$	bp.178℃/0.3mmHg	47
15			$-CH_2C\ell$	bp.202℃/0.1mmHg	55
16			$-CH_2OCH_3$	bp.162℃/0.25mmHg	73
17			$-CH_2C\ell$	bp.168℃/0.2mmHg	96
18			$-CHCH_3$ (Cℓ)	bp.132℃/0.2mmHg	47
19			$-CH_2C\ell$	bp.151℃/0.25mmHg	85
20			$-CH_2C\ell$	bp.161℃/0.2mmHg	80
21			$-CH_2C\ell$	bp.172℃/0.35mmHg	63
22			$-CH_2CH_2C\ell$	bp.141℃/0.35mmHg	45
23			$-CH_2C\ell$	bp.157℃/0.4mmHg	53

Table 1 (continued)

24			$-CH_2C\ell$	bp.161℃/0.15mmHg	40
25			$-CH_2C\ell$	mp.67-9℃	80
26			$-CH_2C\ell$	mp.121-3℃	75
27			$-CH_2C\ell$	mp.70-2℃	84
28			$-CH_2C\ell$	mp. 55	71
29			$-CH_2C\ell$	mp.60-2℃	78
30			$-CH_2Br$	bp. 165~170℃/0.5mmHg	90
31			$-CH_2C\ell$	mp.73-6℃	85

EXAMPLE 6

By the same method as described in Examples 1 to 4, N,N-disubstituted carboxylic acid amide compounds were synthesized by using various Schiff bases, silane compounds and carboxylic acid derivatives. The structural formulae and yields of the resulting amide compounds are summarized in Table 2.

In Table 2, R^1, R^2, R^3, M and HSiXYZ show the following.

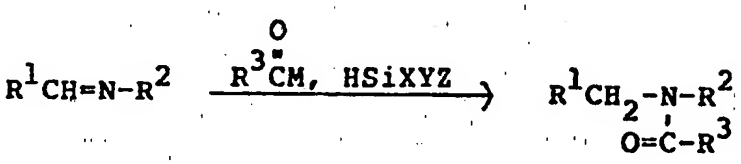


Table 2

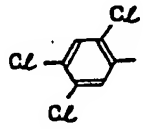
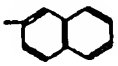
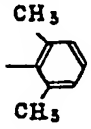
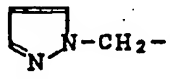
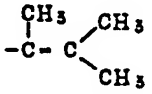
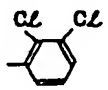
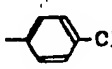
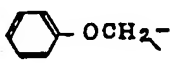
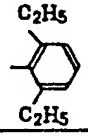
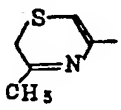
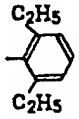
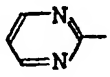
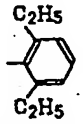
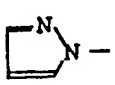
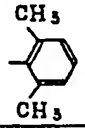
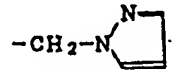
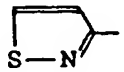
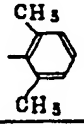
No.	R^1	R^2	R^3	M	HSiXYZ	Yield (%)
1		$-CH_2CH(CH_3)_2$	$-CH-CHCHCH_3$ (Cl)	Cl	$HSiCl_3$	41
2			$-CH_2Cl$	Cl	$HSiCl_3$	55
3			$-CH_2Cl$	Cl	H_2SiCl_2	60
4			$-CH_2Cl$	Cl	$HSiCl_3$	39
5	CH_2-CH-			Cl	$HSiCl_3$	45
6			$-CH_2Cl$	Cl	$HSiCl_3$	50
7			$-CH_2Cl$	Cl	H_2SiCl_2	48
8			$-CH_2Cl$	Cl	$HSiCl_3$	48
9				Cl	$HSiCl_3$	54
10			$-CH_2Cl$	Cl	H_2SiCl_2	60
11		$-CH(CH_3)_2$		Br	$HSiBr_3$	55

Table 2 (continued)

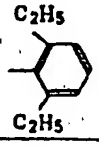
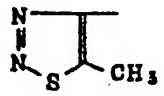
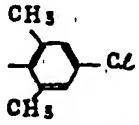
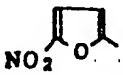
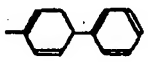
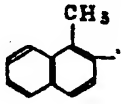
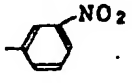
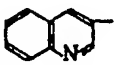
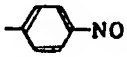
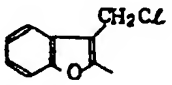
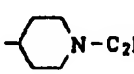
12	$H_5C_2OCCH_2-$ (O)		$-CH_2C\ell$	$C\ell$	$HSiC\ell_3$	42
13	CH_3-	$-C_2H_5$	$-CH_2C\ell$	$C\ell$	$HSiC\ell_3$	70
14	CH_2-CH-	$-CH_2CH-CH_2$	$-CHC\ell_2$	$C\ell$	$H_2SiC\ell_2$	62
15			$-CH_2C\ell$	$C\ell$	$HSiC\ell_3$	38
16		$-CH(CH_3)_2$	$-C(CH_3)_3$	$C\ell$	$H_2SiC\ell_2$	53
17		$\leftarrow CH_2 \rightarrow_4 C\ell$	$-CH_2Br$	Br	$HSiBr_3$	41
18		$-CH_2-$ 	$-CH_2C\ell$	$-OCCH_2C\ell$ (O)	$HSiC\ell_3$	45
19	CH_2-CHCH_2-		$-CH_2CN$	$C\ell$	$HSiC\ell_3$	30
20		$-CH_2C\equiv CH$	$-CH_2CH_2NO_2$	Br	H_2SiBr_2	29
21		$\leftarrow CH_2 \rightarrow_3 SCH_3$		$C\ell$	$H_2SiC\ell_2$	45
22			$-CHC\ell_2$	$C\ell$	$HSiC\ell_3$	60
23			$-CH_2CH_3$	$-OCC_2H_5$ (O)	$H_3SiC\ell$	35

Table 2 (continued)

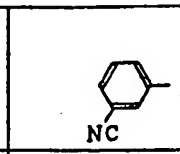
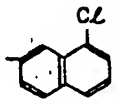
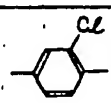
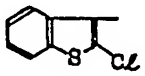
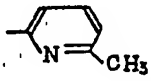
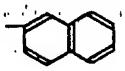
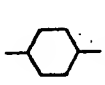
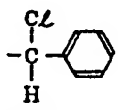
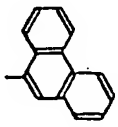
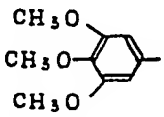
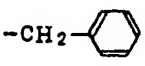
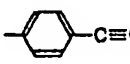
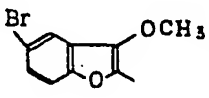
24			$-CF_3$	F	$HSiF_3$	28
25			$-CH_2I$	Cℓ	$H_2SiCℓ_2$	35
26		$\leftarrow CH_2\rightarrow_4 CH=CH_2$	$-CH_2-CH$ 	Cℓ	$H_2SiCℓ_2$	29
27	$-OCH_2CH_2-$		$-CH_2\underset{CH_3}{CH}OC_2H_5$	Cℓ	$H_2SiCℓ_2$	38
28	$(CH_3)_2N-$		$-CH_3$	$-O\overset{O}{\overset{\|}{C}}CH_3$	$HSiCℓ_3$	55
29			$-CH_2Cℓ$	Cℓ	$H_2SiCℓ_2$	40
30	$CH_3-\underset{CH_3}{\overset{CH_3}{C}}-CH_2-$	$-CH_2OC_2H_4$	$-\underset{F}{\overset{CF_3}{C}}OC_5F_7$	F	$HSiBr_3$	25
31	$O_2N\leftarrow CH_2\rightarrow_{10}CH_2-$			Cℓ	$H_2SiCℓ_2$	38
32	CH_3S-		$-CF_3$	$-O\overset{O}{\overset{\|}{C}}CF_3$	$HSiCℓ_3$	48
33		$-CH_2-$ 	$\leftarrow CH_2\rightarrow_4 CN$	Cℓ	$H_3SiCℓ$	65
34			$-CH_2OCH_3$	Cℓ	$HSiCℓ_3$	27
35		$\leftarrow CH_2\rightarrow_9 CH_3$	$-\underset{C_5H_7}{\overset{Cℓ}{CH}}$	Cℓ	$H_2SiCℓ_2$	33

Table 2 (continued)

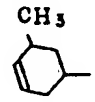
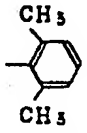
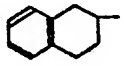
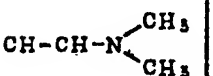
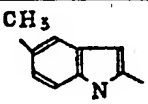
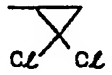
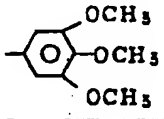
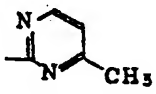
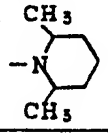
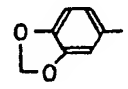
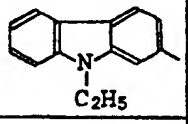
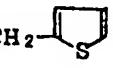
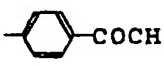
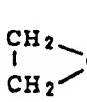
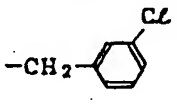
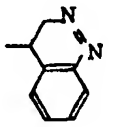
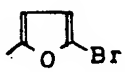
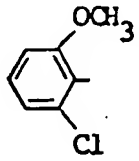
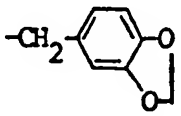
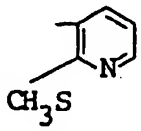
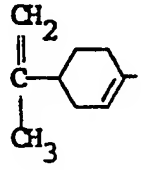
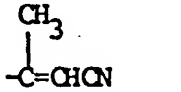
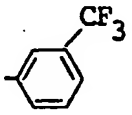
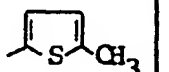
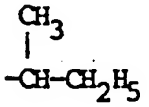
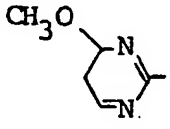
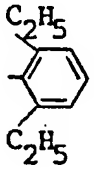
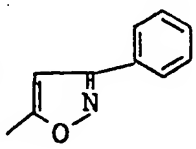
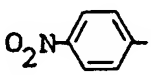
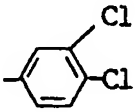
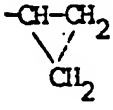
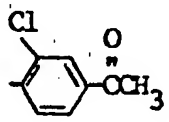
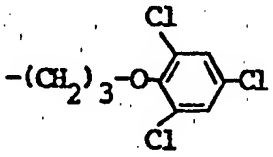
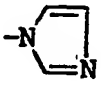
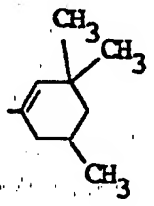
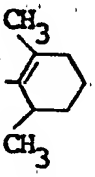
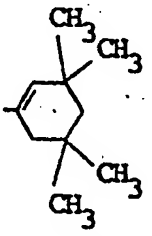
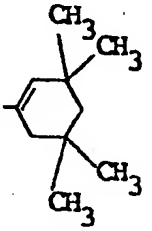
36			$-CH_2CH_3$	$-OC(=O)C_2H_5$	$HSC\ell_3$	45
37			$-CC\ell_2$ 	Cℓ	$H_2SiC\ell_2$	34
38			$-CBr_2H$	Br	H_3SiBr	28
39	$C\ell CH_2CH_2CH_2-$			Cℓ	$HSiC\ell_2$	47
40	$CH_3OCH_2CH_2-$		$-CH_2COCH_3$	Br	H_2SiBr_2	61
41				Cℓ	$H_2SiC\ell_2$	55
42	$CH_3{\equiv}CCH_2-$		$-CH(CH_3)-CH_2$	Cℓ	$H_2SiC\ell_2$	43
43		$-CH_2CH_2-N$ 	$-N$ 	Cℓ	$HSiC\ell_3$	70
44		$-CH_2CH_2OC_2H_5$	$-CH_2-$ 	Cℓ	$HSiC\ell_3$	68
45			$-CH_2CH_2SCH_3$	Br	$HSiBr_3$	48
46				Cℓ	$HSiC\ell_3$	39
47		$-CH_2(CF_2)_2CF_3$		Br	H_2SiBr_2	54

Table 2 (continued)

48				Cl	$HSiCl_3$	41
49			$-CH_2Br$	Br	H_3SiBr	53
50	$NCCH_2CH_2-$			Cl	$HSiCl_3$	57
51			$-CH_2Cl$	Cl	$HSiCl_3$	65
52		$-C_4H_9$	$-CH_2Cl$	Cl	H_2SiCl_2	49
53			$-CH_2Cl$	Cl	$HSiCl_3$	53
54	H		CH_2I	Cl	$HSiCl_3$	58
55				Cl	H_3SiCl	72

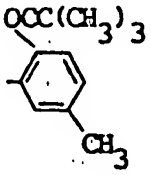
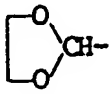
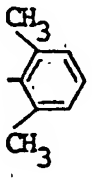
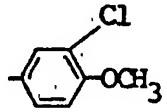
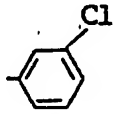
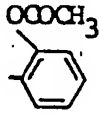
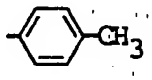
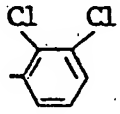
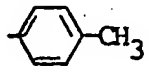
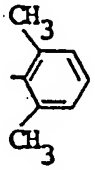
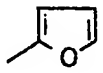
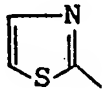
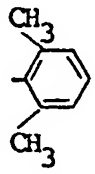
- to be continued -

Table 2 (continued)

56	CH_3-			Cl	$HSiCl_3$	82
57	CH_3CH_2-			Cl	H_2SiCl_2	78
58	$(CH_3)_2CH$-		$-CH_2Cl$	Br	$HSiCl_3$	67
59	CF_3CH_2-		$-CH_2Cl$	Cl	$HSiCl_3$	74
60			$-CH_2Cl$	Br	H_2SiCl_2	59
61	CH≡C-		$-CH_2OCH_3$	Cl	H_2SiCl_2	75
62			$-CHCl_2$	Cl	$HSiCl_3$	63

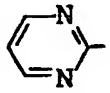
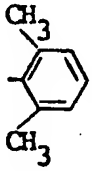
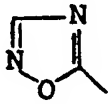
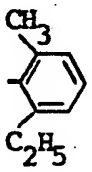
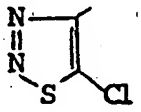
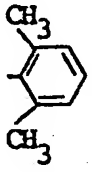
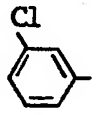
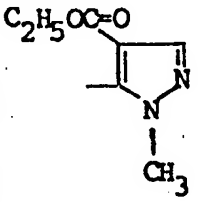
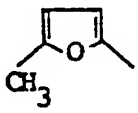
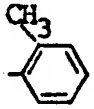
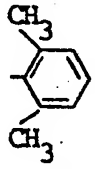
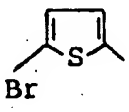
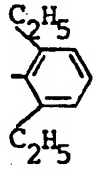
- to be continued -

Table 2 (continued)

63			$-CH_3$	I	H_3SiCl	93
64	H		$-CH_2Cl$		H_2SiCl_2	87
65			$-CH_2Cl$	Cl	H_2SiCl_2	70
66	H			Cl	$HSiCl_3$	92
67	CH_3CH_2-			Cl	H_2SiCl_2	89
68	$CH_2=CH-$			Cl	$HSiCl_3$	78
69	$CH\equiv C-$			Cl	H_2SiCl_2	74
70			$-CH_2Cl$	Br	$HSiCl_3$	91

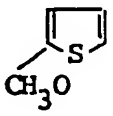
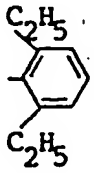
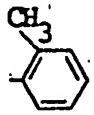
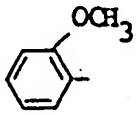
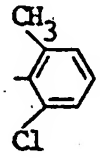
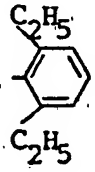
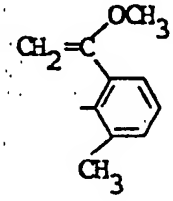
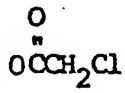
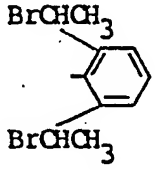
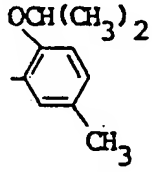
- to be continued -

Table 2 (continued)

71			$-CH_2Cl$	Cl	H_2SiCl_2	75
72			$-CH_2Cl$	Cl	H_2SiCl_2	63
73			$-CH_2Cl$	Cl	H_2SiCl_2	59
74			$-CH_2Cl$	Cl	H_3SiBr	68
75			$-CH_2Cl$		$HSiCl_3$	94
76			$-CH_2Cl$	Cl	H_2SiCl_2	82
77			$-CH_2Cl$	F	$HSiCl_2$	70

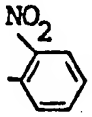
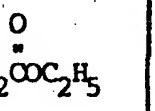
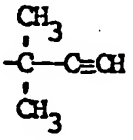
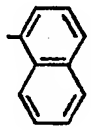
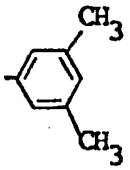
- to be continued -

Table 2 (continued)

78			$-CH_2Cl$	Cl	$HSiCl_3$	91
79			$-CH_2Cl$	Br	$HSiCl_3$	83
80			$-CH_2Cl$	Cl	$HSiCl_3$	95
81	CH_3CH_2- CH_2OCH_2-		$-CH_2Cl$	Cl	H_2SiCl_2	88
82	CH_3		$-CH_2Cl$		H_2SiCl_2	51
83	H		$-CH_2Cl$	Br	$HSiF_3$	67
84	H		$-CH_2Cl$	Cl	H_2SiCl_2	96

- to be continued -

Table 2 (continued)

85	H			Cl	$HSiCl_3$	86
86	CH_3-		-CH_3	Br	H_2SiBr_2	73
87	$CH_3CH_2CH_2$-	-C_2H_5		Cl	$HSiCl_3$	68
88		-CH_2- 		Br	$HSiBr_3$	71
89	H		-CH_2F	Cl	H_2SiCl_2	59
90		-$CH(CH_3)_2$	-$C(CH_3)_3$	Cl	$HSiCl_3$	62
91		-$CH(CH_3)_2$		Cl	$HSiCl_3$	84

EXAMPLE 7

N,N-disubstituted carboxylic acid amide compounds were synthesized in the same way as in Example 6 except that Schiff base compounds of the following formula were used. The results are shown in Table 3.

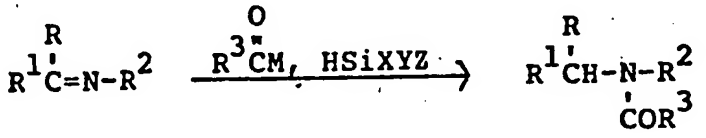
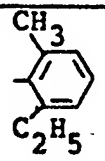
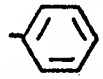
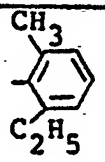
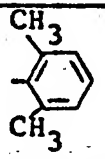
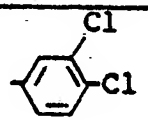
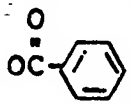
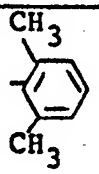
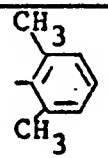
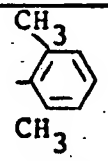
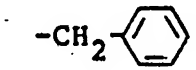
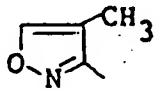
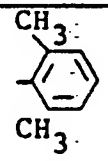
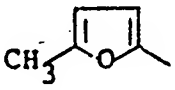
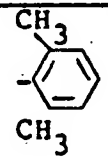
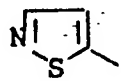
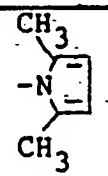
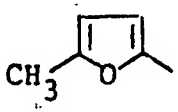


Table 3

No.	R	R_1	R_2	R_3	M	HSiXYZ	Yield (%)
1	CH_3-	CH_3OCH_2-		$-CH_2Cl$	$OCCH_2Cl$	H_2SiCl_2	66
2	CH_3-	CH_3-		$-CH_2Cl$	Br	H_2SiCl_2	73
3	$CH_2=CH-$	CH_3OCH_2-		$-CH_2Cl$	F	H_2SiF_2	62
4	CH_3C-	CH_3-		$-CH_2Cl$	Cl	$HSiCl_3$	67
5	C_2H_5OC-	CH_3-				$HSiCl_3$	59
6	CH_3OC-	CH_3-		$-CH_2OCH_3$	Cl	H_2SiCl_2	75

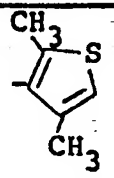
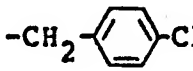
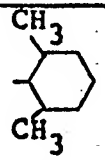
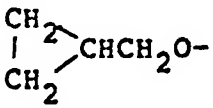
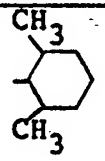
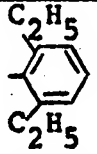
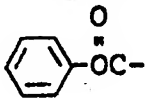
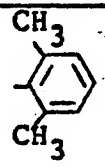
- to be continued -

Table 3 (continued)

7	$CH_3OC(=O)-$	CH_3-			Cl	$HSiCl_3$	63
8	$CH_3OC(=O)-$	CH_3-			Cl	$HSiCl_3$	80
9	CH_3-			$-CH_2Cl$	$OCCH_2Cl$	H_2SiCl_3	64
10	CCl_3-			$-CH_2Cl$	Cl	H_3SiCl	58
11	CH_3-			$-CH_2Cl$	Br	$HSiCl_3$	77
12	CH_3-		$-C_2H_5$	$-CH_2Cl$	Cl	$HSiCl_3$	67

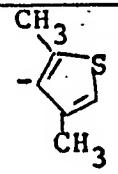
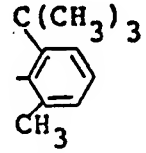
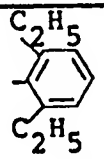
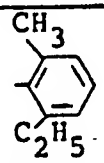
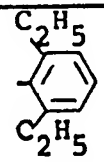
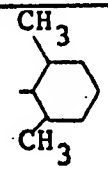
- to be continued -

Table 3 (continued)

13	$CH_3OC(=O)-$	CH_3-		$-CH=CHCH_3$	Cl	H_2SiCl_2	56
14	CH_3O-	H		$-CH=CHCHCH_3$ (Cl)	Cl	$HSiCl_3$	78
15	C_2H_5O-	H		$-CH_2Cl$	Cl	$HSiCl_3$	85
16		H		$-CH_2Cl$	I	$HSiCl_3$	66
17	$C_2H_5OC(=O)-$	H		$-CH_2Cl$	Cl	H_2SiCl_2	80
18		H		$-CH_2Cl$	Cl	$HSiCl_3$	93

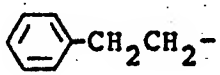
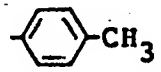
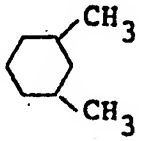
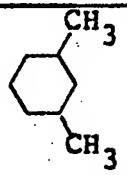
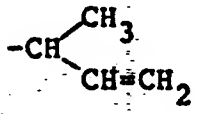
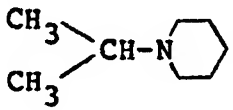
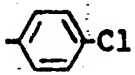
- to be continued -

Table 3 (continued)

19	C_2H_5O-	H		-CH_2Cl	Cl	H_2SiCl_2	88
20	CH_3O-	H		-CH_2Br	Br	H_2SiBr_2	62
21	$CH_3CH_2CH_2CH_2O$-	H		-CH_2Cl	Cl	$HSiCl_3$	81
22	C_2H_5O-	H		-CH_2Cl	$OCCH_2Cl$	H_2SiCl_2	74
23	CH_3O-	H		-CH_2Cl	Cl	$HSiCl_3$	89
24	$CH_2=CHCH_2O$-	H		-CH_2Cl	Cl	H_2SiCl_2	57

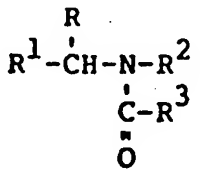
- to be continued -

Table 3 (continued)

25	C_6H_{13}-	C_6H_{13}-	$-C_4H_9$	$-CH_2Cl$	Cl	$HSiCl_3$	71
26	C_4H_9-			$-CH_2Cl$	Cl	H_2SiCl_2	74
27			$-CH_2CH_2CH_2CH_3$	$-CH_2Cl$	F	$HSiF_3$	76
28				$-CH_2Cl$	Cl	$HSiCl_3$	73
29				$-CH_2$ 	Cl	H_2SiCl_2	66

What is claimed is:

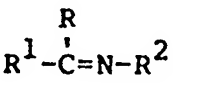
1. A process for producing N,N-disubstituted carboxylic acid amides represented by the following formula (I)



... (I)

wherein R represents a hydrogen atom, an alkyl group, an alkenyl group, an alkoxy group, an alkenyloxy group, a substituted carbonyl group or a trihalogenomethyl group; R^1, R^2 and R^3, independently from each other, represent a substituted or unsubstituted alkyl group, a substituted or unsubstituted alkenyl group, a substituted or unsubstituted alkynyl group, a substituted or unsubstituted aryl group, a substituted or unsubstituted heteroaryl group, a substituted or unsubstituted cycloalkyl group, a substituted or unsubstituted cycloalkenyl group or a substituted or unsubstituted heterocycloalkyl group; R^1 may further represent a hydrogen atom; and R and R^1, taken together, may form a substituted or unsubstituted cyclic group together with the carbon atom to which they are bonded,

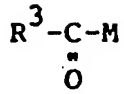
which comprises contacting a Schiff base represented by the following formula (II)



... (II)

wherein R, R^1 and R^2 are as defined above,

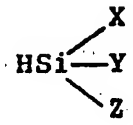
with a carboxylic acid derivative represented by the following formula (III)



... (III)

wherein R^3 is as defined above, and M represents a halogen atom or the moiety $-OCR^3$,

in the presence of a silane compound represented by the following formula (IV)



... (IV)

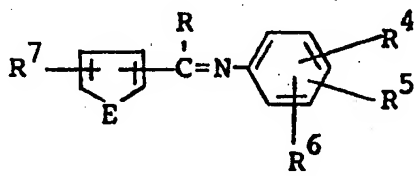
wherein X, Y and Z, independently from each other, represent a hydrogen atom or a halogen atom,

in the presence or absence of an inert organic solvent.

2. The process of claim 1 wherein the contacting is carried out at a temperature in the range of $-20^{\circ}C$ to $150^{\circ}C$.

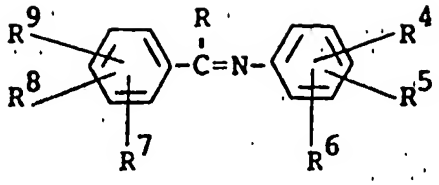
3. The process of claim 1 wherein the amount of the carboxylic acid derivative of formula (III) is 1 to 1.2 moles, and the amount of the silane compound of formula (IV) is 0.25 to 2.2 moles, both per mole of the Schiff base of formula (II).

4. The process of claim 1 wherein the Schiff base of formula (II) is selected from the group consisting of compounds of the following formula



... (II-1)

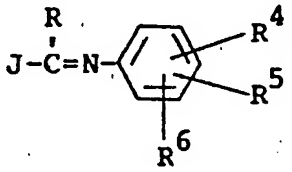
wherein E represents O or S, R is as defined above, R^4, R^5, R^6 and R^7, independently from each other, are the same as defined above for R^1, compounds of the following formula



... (II-2)

wherein R is as defined above, and R^4, R^5, R^6, R^7, R^8 and R^9, independently from each other, are the same as defined above for R^1,

compounds of the following formula

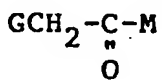


... (II-3)

wherein J represents an alkyl group, an alkoxy group, an alkoxyalkyl group or an alkoxycarbonyl group, R is the same as defined above, and R^4, R^5 and R^6, independently from each other, are the same as defined above for R^1.

5. The process of claim 1 wherein the carboxylic acid derivative of formula (III) is selected from the group consisting of

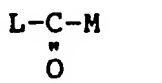
compounds of the formula



... (III-1)

wherein M is as defined above, and G represents a hydrogen atom, a halogen atom, an alkyl group or an alkoxy group.

Compounds of the formula



... (III-2)

wherein M is as defined, and L represents a phenyl group, a pyridyl group, a furyl group or a benzyl group.

6. The process of claim 1 wherein R is a member selected from the class consisting of a hydrogen atom, alkyl groups having 1 to 10 carbon atoms, alkenyl groups having 2 to 6 carbon atoms, alkoxy groups having 1 to 6 carbon atoms, alkenyloxy groups having 2 to 6 carbon atoms, alkylcarbonyl groups having 1 to 8 carbon atoms in the alkyl moiety, alkoxycarbonyl groups having 1 to 8 carbon atoms in the alkoxy moiety, arylcarbonyl groups having substituted or unsubstituted C_6-C_{10} aryl, said substituent for aryl being selected from alkyl groups having 1 to 6 carbon atoms, alkenyl groups having 2 to 6 carbon atoms, alkynyl groups having 2 to 6 carbon atoms, alkoxy groups having 1 to 6 carbon atoms, alkylthio groups having 1 to 6 carbon atoms, alkoxycarbonyl groups having 1 to 4 carbon atoms in the alkoxy moiety, alkylcarbonyl groups having 1 to 4 carbon atoms in the alkyl moiety, halogen atoms, a cyano group, a nitro group, dialkylamino groups having 1 to 4 carbon atoms in each alkyl moiety, trihalogenomethyl groups and alkylcarbonyloxy groups having 1 to 4 carbon atoms in the alkyl moiety, and trihalogenomethyl groups in which the halogen is selected from Cl, Br and F.

7. The process of claim 1 wherein each of R^1, R^2 and R^3 is a member selected from the class consisting of substituted or unsubstituted alkyl groups having 1 to 15 carbon atoms, substituted or unsubstituted alkenyl groups having 2 to 15 carbon atoms, substituted or unsubstituted alkynyl groups having 2 to 15 carbon atoms, substituted or unsubstituted aryl groups having 6 to 20 carbon atoms, substituted or unsubstituted heteroaryl groups having 2 to 20 carbon atoms and 1 to 4 hetero atoms selected from N, N, O and S, substituted or unsubstituted cycloalkyl groups having 3 to 20 carbon atoms, substituted or unsubstituted cycloalkenyl groups having 3 to 20 carbon atoms and substituted or unsubstituted heterocycloalkyl groups having 2 to 20 carbon atoms and 1 to 4 hetero atoms selected from N, O and S; R^1 may further represent a hydrogen atom; R and

R^1, taken together, may form a substituted or unsubstituted C_4-C_{15} cycloalkyl group, or a heterocycloalkyl group, together with the carbon atom to which they are bonded; and the substituents in said substituted groups are selected from alkyl groups having 1 to 6 carbon atoms, alkenyl groups having 2 to 6 carbon atoms, alkynyl groups having 2 to 6 carbon atoms, alkoxy groups having 1 to 6 carbon atoms, alkylthio groups having 1 to 6 carbon atoms, alkoxycarbonyl groups having 1 to 4 carbon atoms in the alkoxy moiety, alkylcarbonyl groups having 1 to 4 carbon atoms in the alkyl moiety, halogen atoms, a cyano group, a nitro group, dialkylamino groups having 1 to 4 carbon atoms in each alkyl moiety, trihalogenomethyl groups and alkylcarbonyloxy groups having 1 to 4 carbon atoms in the alkyl moiety.

European Patent Office

EUROPEAN SEARCH REPORT

0189774
Application number

EP 86 10 0362

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.4)
A	JOURNAL OF ORGANIC CHEMISTRY, vol. 27, July 1962, pages 2640-2643; J.H. BILLMAN et al.: "The reductive acylation of Schiff bases using trimethylamine borane. IV" * Table I; Experimental *	1	C 07 B 43/06 C 07 C 102/00 C 07 D 227/00 C 07 D 247/00 C 07 D 269/00 C 07 D 283/00 C 07 D 325/00 C 07 D 333/00

TECHNICAL FIELDS SEARCHED (Int. Cl.4)

C 07 C 102/00

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	13-05-1986	PAUWELS G.R.A.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
O : non-written disclosure
P : intermediate document

T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO Form 1503. 03.82